

REMARKS

Claims 1, 3-11, 13-15, 17-22 and 24 are currently pending in the present application. No claim amendments have been made in the present response. Reconsideration on the merits is kindly requested in view of the following remarks.

Substance of the Examiner Interview

Applicants kindly thank Examiners Souroush and Richter for the courtesy of conducting an Examiner Interview with Applicants' representative on May 14, 2009. Applicants acknowledge that the Examiners have indicated that the rejection under 35 U.S.C. 112 will be withdrawn. With respect to the outstanding obviousness rejection, Applicants believe that the remarks below will remove any necessity to submit evidence in support of the presently claimed invention.

Rejection under 35 U.S.C. §112, second paragraph

Claims 1, 3-11, 13-15, 17 and 24 stand rejected as being indefinite because of the phrases "good solvents" and "poor solvents".

Per the Examiner's Interview Summary, the outstanding rejection has been withdrawn.

Rejection under 35 U.S.C. §103 – Obviousness

Claims 1, 3-11, 13-15, 17 and 24 stand rejected under 35 U.S.C. § 103 as being unpatentable over USP Publication 2004/0245662 to Chaubal et al. (hereinafter “Chaubal”) in view of USP 2,652,234 to Feldmann. Applicants respectfully traverse.

Legal Standard for Determining Prima Facie Obviousness

To establish a *prima facie* case of obviousness, three basic criteria must be met. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art reference (or references when combined) must teach or suggest all the claim limitations.

The teaching or suggestion to make the claimed combination and the reasonable expectation of success must both be found in the prior art, not in applicant's disclosure. *In re Vaeck*, 947 F.2d 488, 20 USPQ2d 1438 (Fed. Cir. 1991).

“There are three possible sources for a motivation to combine references: the nature of the problem to be solved, the teachings of the prior art, and the knowledge of persons of ordinary skill in the art.” *In re Rouffet*, 149 F.3d 1350, 1357, 47 USPQ2d 1453, 1457-58 (Fed. Cir. 1998) (The combination of the references taught every element of the claimed invention, however without a motivation to combine, a rejection based on a *prima facie* case of obvious was held improper.).

“In determining the propriety of the Patent Office case for obviousness in the first instance, it is necessary to ascertain whether or not the reference teachings would appear to be sufficient for one of ordinary skill in the relevant art having the reference before him to make the proposed substitution, combination, or other modification.” *In re Linter*, 458 F.2d 1013, 1016, 173 USPQ 560, 562 (CCPA 1972).

Obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either explicitly or implicitly in the references themselves or in the knowledge generally available to one of ordinary skill in the art. “The test for an implicit showing is what the combined teachings, knowledge of one of ordinary skill in the art, and the nature of the problem to be solved as a whole would have suggested to those of ordinary skill in the art.” *In re Kotzab*, 217 F.3d 1365, 1370, 55 USPQ2d 1313, 1317 (Fed. Cir. 2000). See also *In re Lee*, 277 F.3d 1338, 1342-44, 61 USPQ2d 1430, 1433-34 (Fed. Cir. 2002) (discussing the importance of relying on objective evidence and making specific factual findings with respect to the motivation to combine references); *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988); *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992).

The Supreme Court of the United States has recently held that the teaching, suggestion, motivation test is a valid test for obviousness, but one which cannot be too rigidly applied. See *KSR Int'l Co. v Teleflex Inc.*, 127 SCt 1727, 82 USPQ2d 1385 (U.S. 2007). The Supreme Court in *KSR Int'l Co. v. Teleflex, Inc.*, *ibid.*, reaffirmed the Graham factors in the determination of obviousness under 35 U.S.C. § 103(a). The four factual inquiries under Graham are:

- (a) determining the scope and contents of the prior art;

- (b) ascertaining the differences between the prior art and the claims in issue;
- (c) resolving the level of ordinary skill in the pertinent art; and
- (d) evaluating evidence of secondary consideration.

Graham v. John Deere, 383 U.S. 1, 17-18, 148 USPQ 459, 467 (U.S. 1966).

The Court in *KSR Int'l Co. v. Teleflex, Inc.*, *supra.*, did not totally reject the use of "teaching, suggestion, or motivation" as a factor in the obviousness analysis. Rather, the Court recognized that a showing of "teaching, suggestion, or motivation" to combine the prior art to meet the claimed subject matter could provide a helpful insight in determining whether the claimed subject matter is obvious under 35 U.S.C. § 103(a).

Even so, the Court in *KSR Int'l Co. v. Teleflex, Inc.*, *ibid.*, rejected a rigid application of the "teaching, suggestion, or motivation" (TSM) test, which required a showing of some teaching, suggestion, or motivation in the prior art that would lead one of ordinary skill in the art to combine the prior art elements in the manner claimed in the application or patent before holding the claimed subject matter to be obvious.

Accordingly, while the courts have adopted a more flexible teaching, suggestion, motivation (TSM) test in connection with the obviousness standard based on the *KSR v. Teleflex* case, which case involved a mechanical device in a relatively predictable technological area, it remains true that, despite this altered standard, the courts recognize inventors face additional barriers in relatively unpredictable technological areas as noted in *Takeda Chemical Industries, Ltd. v. Alphapharm Pty., Ltd.*, 83 USPQ2d 1169 (Fed. Cir. 2007).

Additionally, MPEP § 2143.03 clearly directs that all claim limitations must be considered in view of the cited prior art in order to establish a prima facie case of obviousness.

Distinctions Over the Cited Prior Art

Applicants respectfully submit that the cited prior art fails to provide any teaching or reason or rationale to those of ordinary skill in the art that would allow them to arrive at the instant invention as claimed.

The Examiner has noted two important differences between the present invention and Chaubal – (a) Chaubal does not disclose circulating the poor solvent into the homogenizer and then adding the drug-containing solution to the circulating solution; and (b) Chaubal does not teach a homogenizer with an online injector.

With respect to difference (a), Applicants respectfully submit that the Examiner has not provided any rationale for concluding that the recited order of mixing is obvious. With respect to difference (b), the Examiner has turned to Feldmann, which teaches a homogenizer with an online injector.

However, in accordance with the Examination Guidelines as set forth at MPEP 2141,

The key to supporting any rejection under 35 U.S.C. 103 is the ***clear articulation of the reason(s) why the claimed invention would have been obvious***. The Supreme Court in *KSR* noted that the analysis supporting a rejection under 35 U.S.C. 103 should be made explicit. The Court quoting *In re Kahn*, 441 F.3d 977, 988, 78 USPQ2d 1329, 1336 (Fed. Cir. 2006), stated that ***"[R]ejections on obviousness cannot be sustained by mere conclusory statements; instead, there must be some articulated reasoning with some rational underpinning to support the legal conclusion of obviousness."*** 127 S. Ct. 1727, 1741, 82 USPQ2d 1385, 1396 (2007).

Applicants respectfully submit that the outstanding rejection is improperly based upon conclusory statements without the requisite rational underpinning to support the Examiner's

erroneous conclusion of obviousness. Accordingly, the outstanding obviousness rejection cannot be sustained.

Applicants direct the Examiner's attention to the present specification which explains the advantageous results obtained from the present invention. In accordance with the present invention, ultrafine drug particles are produced that are excellent in long-term dispersibility by preventing precipitation and aggregation of drug particles. In particular, the fine drug particles in a solvent produced by the production method according to the present invention have particle sizes held stably without substantial increase with time, in contrast to the conventional drug particles.

Another unexpectedly superior feature of the present invention is that the methods do not require a pretreatment step for adjusting the drug to have an average particle size at a predetermined level or less (generally 100 μm or less) in the production of ultrafine drug particles using a high-pressure homogenizer (high-pressure emulsifier) and can easily and conveniently carry out the treatment with a high-pressure homogenizer.

Additional surprising advantages of the present invention include: production of ultrafine drug particles even at a low energy output; and the ability to mix two solutions which are inherently difficult to mix with each other. See the present specification, at page 18, line 8 – page 21, line 21.

Therefore, as explained above, the outstanding obviousness rejection cannot be sustained because the Examiner has not established a *prima facie* case of obviousness and the present invention possesses unexpectedly superior advantages over the cited prior art that rebut any allegation of obviousness.

Reconsideration and withdrawal of the outstanding rejection are respectfully requested.

Conclusion

In view of the foregoing, Applicants believe the pending application is in condition for allowance. A Notice of Allowance is earnestly solicited.

Should there be any outstanding matters that need to be resolved in the present application, the Examiner is respectfully requested to contact Monique T. Cole, Reg. No. 60,154 at the telephone number of the undersigned below, to conduct an interview in an effort to expedite prosecution in connection with the present application.

If necessary, the Commissioner is hereby authorized in this, concurrent, and future replies to charge payment or credit any overpayment to Deposit Account No. 02-2448 for any additional fees required under 37.C.F.R. §§1.16 or 1.17; particularly, extension of time fees.

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Respectfully submitted,

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